Claims

1. Use of an agent comprising filamentous haemagglutinin (FHA) or a derivative or mutant or fragment or variant or peptide thereof for the prophylaxis and/or treatment of an immune-mediated disorder.

2. Use of an agent comprising filamentous haemagglutinin (FHA) or derivative or mutant or fragment or variant or peptide thereof for the prophylaxis and/or treatment of an autoimmune disease.

3. Use as claimed in claim 1 or 2 wherein the filamentous haemagglutinin (FHA) is derived from *Bordetella pertussis* or *Bordetella bronchisepetica* or *Bordetella parapertussis* or related molecules from other bacteria.

4. Use as claimed in any of claims 1 to 3 wherein the agent comprises FHA or derivative or mutant or fragment or variant or peptide thereof or a product of cells activated by these materials.

5. Use as claimed in any of claims 1 to 4 wherein the agent comprises FHA in combination with self or foreign antigens or peptides thereof.

6. Use as claimed in any of claims 1 to 5 wherein the agent promotes the generation of Tr cells in response to a self antigen.

7. Use as claimed in any preceding claim wherein FHA acts as an immunomodulator *in vivo* to promote the induction of Tr cells to co-administered self or foreign antigens.

8. Use as claimed in any of claims 4 to 7 wherein the self antigen is selected from any one or more of glutamic acid decarboxylase 65 (GAD 65), native DNA, myelin basic protein, myelin proteolipid protein, acetylcholine receptor

components, thyroglobulin, thyroid stimulating hormone (TSH) receptor, Japanese cedar pollen antigens, ragweed pollen antigens, rye grass pollen antigens, and dust mite antigens and feline antigens for animal, histocompatibility antigens, antigens involved in graft rejection and an altered peptide ligand.

9. Use as claimed in claim 8 wherein the antigens involved in graft rejection comprise antigenic components of the graft to be transplanted into the heart, lung, liver, pancreas, kidney of graft recipients and neural graft components.

10. Use as claimed in any of claims 4 to 9 wherein the self antigen is selected from any one or more of a myelin protein, beta amyloid protein, amyloid precursor protein and collagen and peptides thereof.

11. Use as claimed in claim 10 wherein the myelin protein is myelin basic protein or peptides thereof.

12. Use as claimed in claim 11 wherein the myelin basic protein is myelin oligodendrocyte glycoprotein synthetic peptide.

13. Use as claimed in claim 12 wherein the myelin basic protein is a MOG peptide (35-55).

14. Use as claimed in any preceding claim wherein the agent modulates pro-inflammatory cytokine production.

15. Use as claimed in any preceding claim wherein the agent promotes the induction of anti-inflammatory cytokines.

16. Use as claimed in any preceding claim wherein the immunomodulatory effects of FHA on cells of the innate immune system is enhanced by co-activation with a Toll-like receptor ligand.

17. Use as claimed in claim 16 wherein the Toll-like receptor ligand is LPS or another toll-like receptor ligand, selected from any one or more of CpG motifs, dsRNA, Poly (I:C) and Pam3Cys.

18. Use as claimed in any preceding claim wherein FHA promotes IL-10 and TGF- β production by macrophages and dendritic cells.

19. Use as claimed in any preceding claim wherein FHA promotes IL-6 production by macrophages and dendritic cells.

20. Use as claimed in any preceding claim wherein FHA synergises with LPS to promote IL-10, TGFβ and IL-6 production by macrophages and dendritic cells.

21. Use as claimed in any preceding claim wherein FHA induces expression of TGFβ mRNA.

22. Use as claimed in any preceding claim wherein FHA inhibits inflammatory cytokines, chemokines or other inflammatory mediators.

23. Use as claimed in claim 22 wherein the inflammatory cytokine is selected from any one or more of TNF-α, IFN-γ, IL-2, IL-12, IL-1, IL-23 and IL-27.

24. Use as claimed in claim 22 wherein the inflammatory chemokine is macrophage inflammatory protein-1α or macrophage inflammatory protein-1β.

25. Use as claimed in any preceding claim wherein FHA promotes dendritic cell maturation into a semi-mature phenotype.

26. Use as claimed in any preceding claim wherein FHA promotes dendritic cell maturation following co-activation with TLR-ligands.

27. Use as claimed in any preceding claim wherein FHA inhibits TLR-ligand-induced dendritic cell activation.

28. Use as claimed in any preceding claim wherein FHA is substantially endotoxin free.

29. Use as claimed in any preceding claim wherein FHA is in the form of an immmunomodulator, adjuvant, immunotherapeutic or anti-inflammatory agent.

30. Use as claimed in any preceding claim wherein the agent modulates inflammatory cytokine production induced by infection or trauma.

31. Use as claimed in any preceding claim wherein the immune-mediated disorder is sepsis or acute inflammation induced by infection, trauma or injury.

32. Use as claimed in any preceding claim wherein the immune-mediated disorder is multiple sclerosis.

33. Use as claimed in any preceding claim wherein the immune-mediated disorder is selected from any one or more of multiple sclerosis, Crohn's disease, inflammatory bowel disease, type 1 diabetes, rheumatoid arthritis and psoriasis.

34. Use as claimed in any preceding claim wherein the immune-mediated disorder is colitis.

35. Use as claimed in any preceding claim wherein the immune-mediated disorder is asthma or atopic disease.

36. Use as claimed in any preceding claim in wherein the agent is in a form for oral, intranasal, intravenous, intradermal, subcutaneous or intramuscular administration.

37. Use as claimed in claim 36 comprising repeated administration of the agent.

38. A product comprising FHA or derivative or mutant or fragment or variant or peptide thereof in combination with an antigen, where said antigen is selected from a self-antigen and a foreign antigen.

39. A product comprising FHA or derivative or mutant or fragment or variant or peptide thereof in combination with a TLR ligand.

40. A product comprising FHA or derivative or mutant or fragment or variant or peptide thereof in combination with a TLR ligand and a self antigen.

41. A product as claimed in claim 39 or 40 wherein the TLR ligand is a pharmaceutically acceptable TLR ligand.

42. A product as claimed in any of claims 39 to 41 wherein the TLR ligand is selected from any one or more of CpG motifs, dsRNA, Poly (I:C) and Pam3Cys.

43. A product as claimed in any of claims 38 to 42 wherein FHA comprises a derivative or mutant or fragment or variant or peptide thereof or a product of cells activated by these materials.

44. A product as claimed in any of claims 38 to 43 wherein the self antigen is selected from any one or more of glutamic acid decarboxylase 65 (GAD 65), native DNA, myelin basic protein, myelin proteolipid protein, acetylcholine receptor components, thyroglobulin, thyroid stimulating hormone (TSH) receptor, Japanese cedar pollen antigens, ragweed pollen antigens, rye grass pollen antigens, and dust mite antigens and feline antigens for animal, histocompatibility antigens, antigens involved in graft rejection and an altered peptide ligand.

45. A product as claimed in claim 44 wherein the antigens involved in graft rejection comprise antigenic components of the graft to be transplanted into the heart, lung, liver, pancreas, kidney of graft recipients and neural graft components.

46. A product as claimed in any of claims 38 to 45 wherein the self antigen is selected from any one or more of a myelin protein, beta amyloid protein, amyloid precursor protein and collagen and peptides thereof.

47. A product as claimed in claim 46 wherein the myelin protein is myelin basic protein or peptides thereof.

48. A product as claimed in claim 47 wherein the myelin basic protein is myelin oligodendrocyte glycoprotein synthetic peptide.

49. A product as claimed in claim 48 wherein the myelin basic protein is a MOG peptide (35-55).

50. A pharmaceutical composition comprising FHA or derivative or mutant or fragment or variant or peptide thereof.

51. A pharmaceutical composition comprising FHA or derivative or mutant or fragment or variant or peptide thereof as adjuvant for immunization with a self or foreign antigen.

52. A pharmaceutical composition comprising FHA or derivative or mutant or fragment or variant or peptide thereof in combination with an antigen, where said antigen is selected from a self-antigen and a foreign antigen.

53. A product as claimed in any of claims 50 to 52 wherein FHA comprises a derivative or mutant or fragment or variant or peptide thereof or a product of cells activated by these materials.

54. A pharmaceutical composition as claimed in claim 51 to 53 wherein the self antigen is selected from any one or more of glutamic acid decarboxylase 65 (GAD 65), native DNA, myelin basic protein, myelin proteolipid protein, acetylcholine receptor components, thyroglobulin, thyroid stimulating hormone (TSH) receptor, Japanese cedar pollen antigens, ragweed pollen antigens, rye grass pollen antigens, and dust mite antigens and feline antigens for animal, histocompatibility antigens, antigens involved in graft rejection and an altered peptide ligand.

55. A pharmaceutical composition as claimed in claim 54 wherein the antigens involved in graft rejection include antigenic components of the graft to be transplanted into the heart, lung, liver, pancreas, kidney for graft recipients and neural graft components.

56. A pharmaceutical composition as claimed in any of claims 51 to 55 wherein the self antigen is selected from any one or more of a myelin protein, beta amyloid protein, amyloid precursor protein and collagen and peptides thereof.

57. A pharmaceutical composition as claimed in claim 56 wherein the myelin protein is myelin basic protein or peptides thereof.

58. A pharmaceutical composition as claimed in claim 57 wherein the myelin basic protein is myelin oligodendrocyte glycoprotein synthetic peptide.

59. A pharmaceutical composition as claimed in claim 58 wherein the myelin basic protein is a MOG peptide (35-55).

60. A pharmaceutical composition comprising FHA or derivative or mutant or fragment or variant or peptide thereof in combination with a TLR ligand.

61. A pharmaceutical composition as claimed in claim 60 wherein the TLR ligand is a pharmaceutically acceptable TLR ligand.

62. An immunomodulator comprising FHA or derivative or mutant or fragment or variant or peptide thereof.

63. A recombinant FHA having immunomodulatory effects.

64. A vaccine comprising FHA or derivative or mutant or fragment or variant or peptide thereof.

65. A vaccine as claimed in claim 64 comprising FHA or derivative or mutant or fragment or variant or peptide thereof and an antigen.

66. A vaccine as claimed in claim 65 wherein the FHA and antigen are present in a by weight ratio range of 0.01:1 to 100:1.

67. A vaccine as claimed in claim 65 wherein the FHA and antigen are present in a molar ratio of 1:10 to 10:1.

68. Antibodies to FHA or derivative or mutant or fragment or variant or peptide thereof.

69. A method for preparing a substantially pure preparation of FHA comprising the steps of dialysing a preparation of FHA to denature the protein and expose contaminating endotoxin and removing residual contaminating endotoxin.

70. A method as claimed in claim 69 wherein the contaminating endotoxin is LPS.

71. A method as claimed in claim 69 or 70 wherein the endotoxin is removed using a detergent.

72. A method as claimed in any of claims 69 to 71 comprising the steps of;

priming a purification column;

adding the dialysed FHA preparation;

washing with detergent; and

eluting a substantially purified protein.

73. A method for the prophylaxis and/or treatment of an immune-mediated disorder comprising the step of administering an agent comprising filamentous haemagglutinin (FHA) or a derivative or mutant or fragment or variant or peptide thereof.

74. A method for the prophylaxis and/or treatment of an autoimmune disease comprising the step of administering an agent comprising filamentous haemagglutinin (FHA) or derivative or mutant or fragment or variant or peptide thereof.

75. A method as claimed in claim 73 or 74 wherein the filamentous haemagglutinin (FHA) is derived from *Bordetella pertussis* or *Bordetella bronchisepetica* or *Bordetella parapertussis* or related molecules from other bacteria.

76. A method as claimed in claims 73 to 75 wherein the agent comprises FHA or derivative or mutant or fragment or variant or peptide thereof or a product of cells activated by these materials.

77. A method as claimed in any of claims 73 to 76 wherein the agent comprises FHA in combination with self or foreign antigens or peptides thereof.

78. A method as claimed in any of claims 73 to 77 wherein the agent promotes the generation of Tr cells in response to a self antigen.

79. A method as claimed in any of claims 73 to 78 wherein FHA acts as an immunomodulator *in vivo* to promote the induction of Tr cells to co-administered self or foreign antigens.

80. A method as claimed in any of claims 76 to 79 wherein the self antigen is selected from any one or more of glutamic acid decarboxylase 65 (GAD 65), native DNA, myelin basic protein, myelin proteolipid protein, acetylcholine receptor components, thyroglobulin, thyroid stimulating hormone (TSH) receptor, Japanese cedar pollen antigens, ragweed pollen antigens, rye grass pollen antigens, and dust mite antigens and feline antigens for animal,

histocompatibility antigens, antigens involved in graft rejection and an altered peptide ligand.

81. A method as claimed in claim 80 wherein the antigens involved in graft rejection comprise antigenic components of the graft to be transplanted into the heart, lung, liver, pancreas, kidney of graft recipients and neural graft components.

82. A method as claimed in any of claims 76 to 81 wherein the self antigen is selected from any one or more of a myelin protein, beta amyloid protein, amyloid precursor protein and collagen and peptides thereof.

83. A method as claimed in claim 82 wherein the myelin protein is myelin basic protein or peptides thereof.

84. A method as claimed in claim 83 wherein the myelin basic protein is myelin oligodendrocyte glycoprotein synthetic peptide.

85. A method as claimed in claim 84 wherein the myelin basic protein is a MOG peptide (35-55).

86. A method as claimed in any of claims 73 to 85 wherein the agent modulates pro-inflammatory cytokine production.

87. A method as claimed in any of claims 73 to 86 wherein the agent promotes the induction of anti-inflammatory cytokines.

88. A method as claimed in any of claims 73 to 87 wherein the immunomodulatory effects of FHA on cells of the innate immune system is enhanced by co-activation with a Toll-like receptor ligand.

89. A method as claimed in claim 88 wherein the Toll-like receptor ligand is LPS or another toll-like receptor ligand, selected from any one or more of CpG motifs, dsRNA, Poly (I:C) and Pam3Cys.

90. A method as claimed in any of claims 73 to 89 wherein FHA promotes IL-10 and TGF- β production by macrophages and dendritic cells.

91. A method as claimed in any of claims 73 to 90 wherein FHA promotes IL-6 production by macrophages and dendritic cells.

92. A method as claimed in any of claims 73 to 91 wherein FHA synergises with LPS to promote IL-10, TGFβ and IL-6 production by macrophages and dendritic cells.

93. A method as claimed in any of claims 73 to 92 wherein FHA induces expression of TGFβ mRNA.

94. A method as claimed in any of claims 73 to 93 wherein FHA inhibits inflammatory cytokines, chemokines or other inflammatory mediators.

95. A method as claimed in claim 94 wherein the inflammatory cytokine is selected from any one or more of TNF-α, IFN-γ, IL-2, IL-12, IL-1, IL-23 and IL-27.

96. A method as claimed in claim 94 wherein the inflammatory chemokine is macrophage inflammatory protein-1α or macrophage inflammatory protein-1β.

97. A method as claimed in any of claims 73 to 96 wherein FHA promotes dendritic cell maturation into a semi-mature phenotype.

98. A method as claimed in any of claims 73 to 97 wherein FHA promotes dendritic cell maturation following co-activation with TLR-ligands.

99. A method as claimed in any of claims 73 to 98 wherein FHA inhibits TLR-ligand-induced dendritic cell activation.

100. A method as claimed in any of claims 73 to 99 wherein FHA is substantially endotoxin free.

101. A method as claimed in any of claims 73 to 100 wherein FHA is in the form of an immmunomodulator, adjuvant, immunotherapeutic or anti-inflammatory agent.

102. A method as claimed in any of claims 73 to 101 wherein the agent modulates inflammatory cytokine production induced by infection or trauma.

103. A method as claimed in any of claims 73 to 102 wherein the immune-mediated disorder is sepsis or acute inflammation induced by infection, trauma or injury.

104. A method as claimed in any of claims 73 to 103 wherein the immune-mediated disorder is multiple sclerosis.

105. A method as claimed in any of claims 73 to 104 wherein the immune-mediated disorder is selected from any one or more of multiple sclerosis, Crohn's disease, inflammatory bowel disease, type 1 diabetes, rheumatoid arthritis and psoriasis.

106. A method as claimed in any of claims 73 to 105 wherein the immune-mediated disorder is colitis.

107. A method as claimed in any of claims 73 to 106 wherein the immune-mediated disorder is asthma or atopic disease.

108. A method as claimed in any of claims 73 to 107 in wherein the agent is in a form for oral, intranasal, intravenous, intradermal, subcutaneous or intramuscular administration.

109. A method as claimed in claim 108 comprising repeated administration of the agent.